10. GLOSSARY

Absorption—The taking up of liquids by solids, or of gases by solids or liquids.

Acute Exposure—Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

Adsorption Coefficient (K_{oc})—The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd)—The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Asbestos—A group of highly fibrous minerals with separable, long, thin fibers often arranged in parallel in a column or in matted masses (Veblen and Wylie 1993; Zoltai 1979, 1981). Separated asbestos fibers are generally strong enough and flexible enough to be spun and woven, are heat resistant, and are chemically inert (Veblen and Wylie 1993). (See definitions of *fibrous* and *mineral*.) Currently, U.S. regulatory agencies, such as the EPA and OSHA, recognize six asbestos minerals: the serpentine mineral, chrysotile; and five asbestiform amphibole minerals, actinolite asbestos, tremolite asbestos, anthophyllite asbestos, amosite asbestos (also known as asbestiform cummingtonite-grunerite), and crocidolite asbestos(also known as asbestiform riebeckite) (Agency for Toxic Substances and Disease Registry 2001; OSHA 1992). Proposals have been made to update asbestos regulations to include other asbestiform amphibole minerals such as winchite asbestos and richterite asbestos (Meeker et al. 2001; Wylie and Verkouteren 2000). NOTE: Synthetic vitreous fibers are not minerals because they do not have a crystalline molecular structure and are not asbestos.

Asbestosis— Interstitial fibrosis of the pulmonary parenchyma tissue in which asbestos bodies (fibers coated with protein and iron) or uncoated fibers can be detected (American Thoracic Society 1986). Pulmonary fibrosis refers to a scar-like tissue in the lung that does not expand and contract like normal tissue. This makes breathing difficult. Blood flow to the lung may also be decreased, and this causes the heart to enlarge. People with asbestosis have shortness of breath, often accompanied by a persistent cough. Asbestosis is a slow-developing disease that can eventually lead to disability or death in people who have been exposed to high amounts of asbestos over a long period. Asbestosis is not usually of concern to people exposed to low levels of asbestos. For more information, see the *ATSDR Toxicological Profile for Asbestos* (Agency for Toxic Substances and Disease Registry 2001). Asbestosis has not been found in groups of workers involved in the manufacture of synthetic vitreous fibers.

Benchmark Dose (BMD)—Usually defined as the lower confidence limit on the dose that produces a specified magnitude of changes in a specified adverse response. For example, a BMD_{10} would be the dose producing a 10% response, and the benchmark response (BMR) would be 10%. The BMD is determined by modeling the dose response curve in the region of the dose response relationship where biologically observable data are feasible.

Benchmark Dose Model—A statistical dose-response model applied to either experimental toxicological or epidemiological data to calculate a BMD.

Bioconcentration Factor (BCF)—The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Biomarkers—Broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility.

Cancer Effect Level (CEL)—The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen—A chemical capable of inducing cancer.

Case-Control Study—A type of epidemiological study which examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-controlled study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without outcome.

Case Report—Describes a single individual with a particular disease or exposure. These may suggest some potential topics for scientific research but are not actual research studies.

Case Series—Describes the experience of a small number of individuals with the same disease or exposure. These may suggest potential topics for scientific research but are not actual research studies.

Ceiling Value—A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure—Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome. At least one exposed group is compared to one unexposed group.

Cross-sectional Study—A type of epidemiological study of a group or groups which examines the relationship between exposure and outcome to a chemical or to chemicals at one point in time.

Data Needs—Substance-specific informational needs that if met would reduce the uncertainties of human health assessment.

Developmental Toxicity—The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the adverse effects.

Embryotoxicity and Fetotoxicity—Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the

insult occurs. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Environmental Protection Agency (EPA) Health Advisory—An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Epidemiology—Refers to the investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Fiber—Any slender, elongated particle or mineral structure. For the purposes of counting fibrous glass fibers or other synthetic vitreous fibers in air samples, the NIOSH (1994a) 7400B counting rule has sometimes been used: length >5 µm, width <3 µm, and length:width ratio $5:1. The ACGIH (2001) TLV-TWAs for synthetic vitreous fibers are for "respirable" fibers with length >5 µm, and length:width ratios $3:1. For the purposes of counting asbestos fibers in air samples, regulatory agencies commonly count particles that have lengths $5 µm and length:width ratios $3:1 as fibers (NIOSH 1994a; counting rule 7400A). For detecting asbestos fibers in bulk building materials, particles with length:width ratios $5:1 are counted as fibers.

Fiber-year/mL—Epidemiologic studies of groups of workers exposed to airborne inorganic fibers commonly express exposure in cumulative exposure units of fiber-year/mL or fiber-year/cc. This exposure measure is calculated by multiplying a worker's duration of exposure (measured in years) by the average air concentration during the period of exposure (measured in number of fibers/mL of air or fiber/cc). The units are sometimes reported as fiber/month-cc or fiber/year-cc.

Fibrosis, Pulmonary Interstitial—Scar-like tissue that develops in the lung parenchymal tissue in response to inhalation of dusts of certain types of substances such as asbestos and crystalline silica.

Fibrous—Having the slender, elongated shape of a fiber. In mineralogy, fibrous refers to a mineral habit with crystals that look like fibers (Zoltai 1981). A mineral with a fibrous habit is not asbestiform if the fibers are not separable and are not long, thin, strong, and flexible (Veblen and Wylie 1993; Zoltai 1979; 1981).

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic or carcinogenic event because of specific alteration of the molecular structure of the genome.

Half-life—A measure of rate for the time required to eliminate one half of a quantity of a chemical from the body or environmental media.

Immediately Dangerous to Life or Health (IDLH)—The maximum environmental concentration of a contaminant from which one could escape within 30 minutes without any escape-impairing symptoms or irreversible health effects.

Incidence—The ratio of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

Intermediate Exposure—Exposure to a chemical for a duration of 15–364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity—The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

Immunological Effects—Functional changes in the immune response.

***In Vitro*—**Isolated from the living organism and artificially maintained, as in a test tube.

***In Vivo*—**Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC_{LO})—The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50})—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{(LO)}$ (LD_{LO})—The lowest dose of a chemical introduced by a route other than inhalation that has been reported to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50})—The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time$_{(50)}$ (LT_{50})—A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)—The lowest exposure level of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

Malformations—Permanent structural changes that may adversely affect survival, development, or function.

Mesothelioma—Cancer of the thin lining surrounding the lung (the pleura) or the abdominal cavity (the peritoneum). Mesotheliomas are rare cancers in general populations. Mesotheliomas annually accounted for an average of 1.75 deaths per million in the U.S. general population for the period 1987–1996 (NIOSH 1999). For U.S. white males (the U.S. group with the highest mortality rate), the rates were 3.61 per million in 1987 and 2.87 per million in 1996 (NIOSH 1999). See the *ATSDR Toxicological Profile for Asbestos* for more information. Increased risk for mesotheliomas has been associated with occupational exposure to asbestos (Agency for Toxic Substance and Disease Registry 2001), but not with employment in the manufacture of fibrous glass, rock wool, or slag wool (Marsh et al. 2001b).

Mineral—Any naturally occurring, inorganic substance with a crystal structure. Naturally occurring, inorganic substances without a crystal structure (such as amorphous silica and synthetic vitreous fibers) are called mineraloids (Veblen and Wylie 1993).

Minimal Risk Level (MRL)—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.

Modifying Factor (MF)—A value (greater than zero) that is applied to the derivation of a minimal risk level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.

Morbidity—State of being diseased; morbidity rate is the incidence or prevalence of disease in a specific population.

Mortality—Death; mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes mutations. A mutation is a change in the DNA sequence of a cell's DNA. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

Neurotoxicity—The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)—The dose of a chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in *n*-octanol and water, in dilute solution.

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) which represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An odds ratio of greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed.

Organophosphate or Organophosphorus Compound—A phosphorus containing organic compound and especially a pesticide that acts by inhibiting cholinesterase.

Permissible Exposure Limit (PEL)—An Occupational Safety and Health Administration (OSHA) allowable exposure level in workplace air averaged over an 8-hour shift of a 40-hour workweek.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests.

Pharmacokinetics—The science of quantitatively predicting the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism and excretion of chemicals by the body.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments which, in general, do not represent real, identifiable anatomic regions of the body whereby the physiologically-based model compartments represent real anatomic regions of the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically-based dose-response model which quantitatively describes the relationship between target tissue dose and toxic end points. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—Comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information: tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates and, possibly membrane permeabilities. The models also utilize biochemical information such as air/blood partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Pleura—A thin lining or membrane around the lungs or chest cavity. This lining can become thickened or calcified in asbestos-related disease. Pleural abnormalities associated with exposure to asbestos include pleural plaques (localized thickening), pleural thickening or calcifications (widespread thickening), and pleural effusion (see *ATSDR Toxicological Profile for Asbestos*, Agency for Toxic Substance and Disease Registry 2001). Pleural abnormalities have not been a frequent observation in chest x-ray studies of workers involved in the manufacture of fibrous glass, rock wool, or slag wool (Clausen et al. 1993; Gross 1976; Hill et al. 1973; Hughes et al. 1993; Nasr et al. 1971; Weill et al. 1983; Wright 1968).

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Prospective Study—A type of cohort study in which the pertinent observations are made on events occurring after the start of the study. A group is followed over time.

Pulmonary Clearance of Fibers—Clearance of particles or fibers deposited in the lower lung (see definition for *respirable fibers or particles*) involves engulfment (i.e., phagocytosis) by cells called alveolar macrophages. Fiber-containing macrophages are transported to the mucociliary escalator where they can be cleared to the larynx. Results from animal studies and studies of lung tissue from fiber-exposed human subjects indicate that fibers with lengths longer than the diameter of macrophage cells (about 12–20 μm) are not cleared from the lower lung until they dissolve or transversely break, because of the inability of macrophages to fully engulf them (Hesterberg and Hart 2001; Hesterberg et al. 1996; Lippmann 1994). The dissolution and transverse breakage of fibers within cells or interstitial fluids is an important feature of the mechanism by which the lung clears respired fibers (Bernstein et al. 1996; Hesterberg and Hart 2001; Hesterberg et al. 1996; Lippmann 1994). Rates of dissolution of different types of fibers in lung fluid have been correlated with abilities to produce cytotoxicity, lung fibrosis, and cancer (Lippmann 1994).

q_1*—The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Recommended Exposure Limit (REL)—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentrations for up to a 10-hour workday during a 40-hour workweek.

Reference Concentration (RfC)—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime.

The inhalation reference concentration is for continuous inhalation exposures and is appropriately expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the no-observed-adverse-effect level (NOAEL-from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity—The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Respirable Fibers or Particles—Fibers or particles that can be inhaled into the lower lung where gas exchange occurs. The aerodynamic diameter of a particle is a key determinant of its respirability. The formula for aerodynamic diameter (DA) is $DA=1.3xp^{1/2}xd^{5/6}xL^{1/6}$, where p=particle density; d=actual diameter; and L=length (Hesterberg and Hart 2001; Stober 1972). The formula shows that length is much less important than actual diameter in determining aerodynamic diameter. Consistent with this are observations that long fibers with very small diameters can be transported into the lower lung. Asbestos fibers longer than 100 µm have been detected in human (Morgan and Holmes 1980; Timbrell 1972) and rat lungs (Morgan et al. 1978). Fibers or particles with aerodynamic diameters >3–5 µm are expected to be predominantly deposited in the upper airways and not transported to the lower lung (Morgan et al. 1980; Oberdörster 1994). Fibers and particles deposited in the upper airways are quickly cleared to the throat by mucociliary action. Based on a review of the literature on particle deposition in the human lung, ACGIH (2001) published an algorithm predicting the collection efficiency of particles of varying aerodynamic diameters. The algorithm predicts that inhalation exposure to particles of uniform aerodynamic diameters of 1, 5, 6, or 10 µm would lead to the following mass percentages being deposited in the lower lung: 97, 30, 17, or 1%.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Risk—The possibility or chance that some adverse effect will result from a given exposure to a chemical.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic, that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed.

Short-Term Exposure Limit (STEL)—The American Conference of Governmental Industrial Hygienists (ACGIH) maximum concentration to which workers can be exposed for up to 15 minutes continually. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily Threshold Limit Value - Time Weighted Average (TLV-TWA) may not be exceeded.

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Synthetic Vitreous Fibers—Fibers that are manufactured from molten sand, glass, basalt rock, slag (a by-product of certain smelting processes), or clay. The terms *synthetic vitreous fibers, man-made vitreous fibers, or manufactured vitreous fibers* have replaced the earlier term *man-made mineral fibers*, because these fibers are not naturally occurring and do not have a crystalline structure like naturally-occurring mineral fibers such as asbestos fibers. (See definitions for *asbestos*, *fiber*, *mineral*, and *respirable fibers or particles*.) Glass wool, rock (stone) wool, slag wool, and refractory ceramic fibers are made by spinning or blowing the respective molten starting materials of sand or glass, rock, slag, and clay. Continuous filament glass fibers are made by pulling the molten material through small holes.

Target Organ Toxicity—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen—A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a Time Weighted Average (TWA), as a Short-Term Exposure Limit (STEL), or as a ceiling limit (CL).

Time-Weighted Average (TWA)—An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose$_{(50)}$ (TD$_{50}$)—A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Toxicokinetic—The study of the absorption, distribution and elimination of toxic compounds in the living organism.

Uncertainty Factor (UF)—A factor used in operationally deriving the Minimal Risk Level (MRL) or Reference Dose (RfD) or Reference Concentration (RfC) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of one can be used; however a reduced UF of three may be used on a case-by-case basis, three being the approximate logarithmic average of 10 and 1.

Xenobiotic—Any chemical that is foreign to the biological system.